

Abstract

Biodegradable and/or biologically resorbable (continuous) fibres, a method for their preparation and their use as reinforcement fibres

The invention relates to biologically degradable and/or biologically resorbable (continuous) fibres and a method for their preparation. The (continuous) fibres are obtained by partial or complete hydrolytic condensation of one or more hydrolytically condensable silicon compounds and/or precondensates derived therefrom. The hydrolytic condensation is performed under the effect of water and eventually in the presence of a catalyst and/or a solvent and preferably according to a sol-gel-method. With this partial or complete hydrolytic condensation is obtained a spinning mass, which can be processed to continuous and/or long and/or short fibres by conventional methods.

Description

The invention relates to biologically degradable and/or biologically resorbable (continuous) fibres, a method for their preparation and their use as reinforcement fibres.

Organic polymer fibres are used as fibre material in human tissue (US 3,297,033; L. Fambri, A. Pegoretti, M. Mazzurana, C. Migliaresi, J. Mat. Sci.: Materials in Medicine, 5, 1994, 679; P. Ylinen, J. Mat. Sci.: Materials in Medicine, 5, 1994, 522; D. G. Tunc, Clinical Materials 8, 1991, 119; R. A. Olson, D. L. Roberts, D. B. Osbon, Oral. Surg., 53, 1982, 441; J. W. Leenslag, M. T. Kroes, A. J. Pennings, B. Van Cer Lei, New Polym. Mater., 1, 1988, 111; C. M. Agraval, K. F. Haas, D. A. Leopold, H. G. Clark, Biomaterials, 13, 1992, 176; D. H. Lewis in: Biodegradable polymers as drug delivery systems, eds. M. Chasin, R. Langer, Marcel Dekker, New York, 1990, 1; S. H. Hyon, K. Jamshidi, Y. Ikada in Polymers as biomaterials, eds. S. Shalaby, A. S. Hoffmann, B. D. Ratner, T. A. Horbett, Plenum Press, New York, 1984, 51).

However, biologically degradable and/or resorbable materials, that can be used e.g. in surgery, are wanted in the medical technique for fixing eventually broken bones in the human body until the fracture is healed. For fixing are used for example screws, that are prepared of biologically degradable and/or biologically resorbable organic polymers. Their big

advantage compared to traditional metal screws is e.g. the resorbability in the human body after the occurred healing, which usually takes couple of months. Through the resorption of the implant second operations for removing the introduced material are not necessary any more.

Unfortunately, the biologically degradable osteosynthesis materials according to the prior art, that consist e.g. of lactic acid derivatives (polylactides) have, however, a weighty disadvantage. Their mechanical strength is, compared to metal materials, not so high. It is to be expected, that the introduction of reinforcement fibres to the compact material can substantially improve its mechanical strength. However, it is necessary, that the fibres degrade under conditions prevailing in the human organism as fast or as slow, as the polylactide material itself.

According to the prior art unresorbable carbon fibres are used in the preparation of binding materials and for their reinforcement. Such materials are used e.g. for fixations of cords or ligaments. The disadvantage is, however, that the foreign substance, which can cause infections and other negative reactions, remains in the organism.

Metal implants differ in their mechanical characteristics strongly from those of the body tissue and have therefore an additional disadvantage. Metals are substantially stronger than natural bones. This leads in the immediate environment of the metal implant to resorption of bone substance with the result, that the implant loosens. It would be advantageous, if materials would be available, that conform in their mechanical properties with those of the tissue.

Steve T. Lin et al. describe in *Blomaterials* 1994, Vol. 15 No. 13, p 1057 – 1061, biologically absorbable fibres of calcium-iron-phosphate-glasses. They are, however, manufactured by a very energy-intensive and costly melting process.

From DE 29009991 C2 are known silicic acids fibres, which can also be used as reinforcement fibres in fibre bonding materials. The fibres described therein are obtained by handling the water glass fibres with acids or saline solutions, through which the resulting fibres do not contain any additional substances besides SiO_2 and smallish amounts of wa-

ter with the result, that these fibres have only an extremely low degradation rate and can therefore not be used as resorbable material.

DE 3510753 C2 discloses high temperature silicon dioxide fibre material, which is obtained by dry spinning of water glass and by succeeding dehydration and by one hour tempering at 1500°C. This fibre material has a very high SiO₂ content of more than 95 percentage by weight, a density between 1.9 and 2.4 g/cm³ and a content of microcrystalline cristobalite areas from 5% to 10%. These fibres show likewise very slow degradation rates in body-like medias and additionally tissue reactions to the crystalline areas are to be expected, which is not allowed when used in medical technology.

The aim of the present invention is now to prepare biologically degradable and/or biologically resorbable (continuous) fibres, which can be used e.g. as reinforcement fibres for biologically degradable and/or biologically resorbable (implant) materials. The toxicological properties and the biological compatibility of these fibres should be adjustable corresponding to each purpose of use, so that these fibres can also be used in human medicine, if required. Additionally, the resorbability of the fibres should be controllable and adjustable to the requirements of each purpose of use. Thus, there are e.g. different requirements for degradation rates of implants made of binding materials for fast healing tissue and for slow occurring healing processes. The fibres should be suitable for preparation of biologically degradable binding materials, they should be especially usable as reinforcement components in polymers, e.g. polylactide. These binding materials should then be mouldable to screws, plates, bands or sewing material. The fibres should be able to replace carbon fibres and be suitable for preparation of implants (e.g. cords or ligaments), which are fully resorbable in human organism, so that after the resorption there is no foreign substance, that can cause infections or other negative reactions, left in the organism. Additionally, the fibres should be such that the mechanical properties of the binding materials can be adjusted through fibres to those of the tissue in the human organism. The fibres should not only be usable as reinforcement components in binding materials, but also as surgical sewing material.

The aim of the present invention is further to obtain a method, by which biologically degradable and/or biologically resorbable fibres (continuous and/or short fibres) having the above-mentioned properties can be prepared. The method must be devised so, that as a

result fibres having defined mechanical characteristic values are obtained and that continuous as well as long or short fibres can be prepared. The method should further be so variable, that the toxicological properties, the resorbability and the degradation rate of the fibres can be adjusted to the requirements of each purpose of use. Further, the method should not be energy-intensive or costly.

This aim is obtained through (continuous) fibres, which are attained by partial or complete hydrolytic condensation of one or more condensable silica compounds and/or precondensates derived therefrom. The hydrolytic condensation is performed by action of water and eventually in the presence of a catalyst and/or a solvent and preferably according to a sol-gel method.

By this partial or complete hydrolytic condensation a spinning mass is obtained, which is mouldable according to conventional methods to continuous and/or long and/or short fibres.

The fibres according to the invention show, depending on the initial mixture for the spinning mass, round, oval or bone-shaped forms of cross-section. The diameters of the fibres according to the invention are, depending on the spinning conditions, between 5 and 50 μm , preferably between 10 and 20 μm . The cross-section surfaces show values between 100 and 500 μm^2 , preferably between 150 and 250 μm^2 . The fibres according to the invention have tensile strengths of 100 - 800 MPa and E-modules of 15 GPa. The average ultimate elongation of the fibres according to the invention is at circa 2%.

It was unexpectedly found out that the fibres according to the invention are biologically degradable and biologically resorbable and dissolve in weakly basic, body-like fluids having degradation rates between 10 and 100 nm fibre radius per day, whereby the degradation rate correlates with the amount of silanol groups of the fibre. A fibre according to the invention having a diameter of 10 μm is thus completely degraded within 50 - 500 days.

After the complete hydrolysis of the spinning mass the fibres according to the invention have a formal chemical composition $\text{Si}_n(\text{OH})_{2x}\text{O}_{2n-x}$. With the degree or extent of the condensation (polycondensation), i.e. with the amount of the remaining silanol groups the degradation rate and the resorbability of the fibres according to the invention can be controlled

intentionally and adjusted to the requirements of the application in question. The smaller is the extent of the condensation, i.e. the higher is the amount of the remaining OH-groups, the higher is the degradation rate and the higher is the resorbability of the fibres according to the invention.

The fibres according to the invention can be used for preparation of biologically degradable and /or biologically resorbable binding materials, whereby they are introduced e.g. as reinforcement components to biologically degradable and/or resorbable polymers, e.g. to polylactide, polyglycolide, hydroxyapatite, polyesteramide, starch, BIOCELLAT®, polydioxanone, PDS, GELFILM®, Biofix®, TCP, DXO, polyglactin, PLA/PG copolymer or Ca-phosphate. These binding materials produced in this way can be moulded to e.g. screws, plates or bands. Through the combination of biologically degradable, inorganic fibres with biologically degradable polymers biologically degradable materials are prepared, which in their mechanical properties overcome clearly those of the pure polymer compact materials. Herewith is prevented a premature mechanical interference of biologically degradable implants. The fibres according to the invention can substitute carbon fibres, which are used e.g. for repairing of ligaments and bands. For the substitution of the unresorbable carbon fibres with the fibres according to the invention materials for implants (e.g. for ligaments and bands) are now available, which are completely resorbable in the human organism. No foreign substance, which can cause infections or other negative reactions, remains in the organism.

Through the silanol content of the fibres according to the invention their degradation rate and their resorbability can be affected intentionally and thus adjusted to the requirements of the application purpose in question. In case of fast curing tissue, for example, a higher degradation rate of the implanted composite material as in case of more slowly occurring healing processes has to be aimed at. Accordingly, fibres according to the invention have higher silanol content for fast resorbing implants as for those to be resorbed slowly.

The mechanical properties of the fibres according to the invention can also be controlled intentionally through the degree of the hydrolysis and be adjusted to the requirements of each purpose of use. If, for the preparation of the fibres according to the invention silica compounds are used, which have in their molecule at least one organic, hydrolysable

group (e.g. – OC₂H₅), then in the incomplete hydrolysis C₂H₅O groups remain in the fibre, which influence their mechanical properties.

The fibres according to the invention can also be directly used as surgical sewing material. It is also possible to use the fibres according to the invention for preparation of the depots for active agent, whereby the active agents are released gradually during fibre degradation. It is also possible to change the texture of the implants with the aid of the fibres according to the invention so, that the formation of collagen is stimulated through the fibrous surface, so that a stable biological surface is formed on the surface of the implant thus improving its biocompatibility.

The preparation of the spinning mass, i.e. the hydrolytic condensation of the hydrolysable silica compounds is performed preferably through a sol-gel method, as disclosed for example in DE-A1 27 58 414, 27 58 415, 30 11 761, 38 26 715 and 38 35 968. In most cases the hydrolytic condensation can occur in that to the silica compounds to be hydrolysed, which are either as such or as dissolved in a suitable solvent, is directly added the necessary water at the room temperature or under light cooling – preferably by mixing and in the presence of a hydrolysis or condensation catalyst – and in that the resulting mixture is after that mixed for a while (from one to several hours).

For the preparation of spinning mass are preferably used silica compounds of the general formula I,



in which rests X are the same or different and stand for hydroxy, hydrogen, halogen, amino, alkoxy, acyloxy, alkyl carbonyl or alkoxy carbonyl and derive from alkyl rests, which are eventually substituted straight-chain, branched or cyclic rests having 1 to 20 carbon atoms, especially having 1 to 10 carbon atoms and preferably lower alkyl rests having 1 to 6 carbon atoms, and can be interrupted by oxygen or sulphur atoms or by amino groups. Particular examples are methyl, ethyl, n-propyl, i-propyl, n-butyl, i-butyl, s-butyl, t-butyl, n-pentyl, n-hexyl, cyclohexyl, 2-ethylhexyl, dodecyl and octadecyl.

It is likewise possible to use mixtures of silica compounds of the formula I, precondensates derived therefrom or mixtures of monomers and precondensates.

Silans of the formula I are commercially purchaseable or preparable according to the methods as described for example in "Chemie und Technologie der Silicone" (W. Noll, Verlag Chemie, Weinheim, 1968). Without restricting generality concrete examples for compounds of formula I are:

$\text{Si}(\text{OMe})_4$, $\text{Si}(\text{OMe})_3(\text{OEt})$, $\text{Si}(\text{OMe})_2(\text{OEt})_2$, $\text{Si}(\text{OMe})(\text{OEt})_3$, $\text{Si}(\text{OEt})_4$, $\text{Si}(\text{O-i-Pr})_4$,
 $\text{Si}(\text{OMe})_3(\text{O-i-Pr})$, $\text{Si}(\text{OMe})_2(\text{O-i-Pr})_2$, $\text{Si}(\text{OMe})(\text{O-i-Pr})_3$, $\text{Si}(\text{OEt})_3(\text{O-i-Pr})$, $\text{Si}(\text{OEt})_2(\text{O-i-Pr})_2$,
 $\text{Si}(\text{OEt})(\text{O-i-Pr})_3$, $\text{Si}(\text{O-n-Pr})_4$, $\text{Si}(\text{OMe})_3(\text{O-n-Pr})$, $\text{Si}(\text{OMe})_2(\text{O-n-Pr})_2$, $\text{Si}(\text{OMe})(\text{O-n-Pr})_3$,
 $\text{Si}(\text{OEt})_3(\text{O-n-Pr})$, $\text{Si}(\text{OEt})_2(\text{O-n-Pr})_2$, $\text{Si}(\text{OEt})(\text{O-n-Pr})_3$, $\text{Si}(\text{O-i-Pr})_3(\text{O-n-Pr})$, $\text{Si}(\text{O-i-Pr})_2(\text{O-n-Pr})_2$,
 $\text{Si}(\text{O-i-Pr})(\text{O-n-Pr})_3$, $\text{Si}(\text{OMe})(\text{OEt})_2(\text{O-i-Pr})$, $\text{Si}(\text{OMe})(\text{OEt})_2(\text{O-n-Pr})$, $\text{Si}(\text{OMe})(\text{OEt})(\text{O-i-Pr})_2$,
 $\text{Si}(\text{OMe})(\text{O-n-Pr})_2$, $\text{Si}(\text{OMe})(\text{O-i-Pr})(\text{O-n-Pr})_2$,

With preferable embodiments for preparation of the spinning mass such a big amount of water is used for the hydrolysis, that the molar ratio of $\text{SiX}_4 : \text{H}_2\text{O}$ is between 1 : 1 and 1 : 10, preferably between 1 : 1.5 and 1 : 2.5.

If no phase-transfer catalyst is used, preferably a water-soluble solvent (S) or a solvent mixture is used for the preparation of the spinning mass, so that the silica compound(s) and water form a homogenous phase. Without restricting generality examples for suitable solvents are methanol, ethanol, n-propanol, and i-propanol. Mixtures are also possible. It is especially preferable, if the molar ratio S : SiX_4 is at least 1 : 1. If a phase-transfer catalyst is used, the presence of a water-soluble solvent is not absolutely necessary.

For other preferable embodiments for the preparation of the spinning mass the mixture of hydrolysable silica compound, water-soluble solvent, water and catalyst is mixed until a dynamic balance has been adjusted and the hydrolysis has then quasi ended.

Additionally, it is preferable, if for the preparation of the spinning mass, after the ended hydrolysis, solvent is taken away from the resulting mixture until the remaining mixture has in room temperature and in shear rate of 20 s^{-1} a viscosity between 0.05 and $50 \text{ Pa} \cdot \text{s}$, preferably between 0.5 and $\text{Pa} \cdot \text{s}$.

For the preparation of especially homogenous fibres it is preferable, if the spinning mass is exposed to a further filtration before the spinning process.

For the preparation of high-quality continuous fibres of the invention having a flat fibre surface the following procedure for the preparation of the spinning mass has turned out to be particularly preferable. A spinning mass is prepared by hydrolytic (partial) condensation of one or more silica compounds of the general formula I and /or of precondensates derived therefrom by adding water and eventually in the presence of a catalyst, whereby such a big amount of water is used, that the molar ratio $\text{SiX}_4 : \text{H}_2\text{O}$ is between 1 : 1 and 1 : 10, preferably between 1 : 1 and 1 : 1,5. Such a big amount of a water-soluble solvent (S) or a mixture of solvents is used, that the molar ratio is $\text{S} : \text{SiX}_4 \geq 1$. After the terminated hydrolysis and the adjustment of a dynamic balance the S is taken away until the resulting mixture has in room temperature and in shear rate of 20 s^{-1} a viscosity between 0,05 and 50 Pa·s. After the removal of the solvent or the mixture of solvent the resulting mixture is exposed to filtration. It is preferable, if the viscosity is between 0,5 and 3 Pa·s or if the mesh size of the filtration medium is 0,5 to 1,5 mm. It is especially preferable, if the filtration medium has a mesh size of 1 mm. After the filtration the resulting mixture is allowed to stand until it obtains spinnability. Depending on the temperature the ripening time is between several hours (e.g. 6 hours) and several months and is determined by the residual content of the solvent or mixture of solvent. After the termination of the ripening time a homogenous, readily mouldable spinning mass is obtained, which remains stable and thus spinnable for a while (from 30 minutes to some hours), before it gelates. The spinning mass is moulded to threads, which are also eventually dried.

In this way particularly homogenous continuous fibres are obtained.

The fibres prepared in this way can also comprise hydrolysable groups X, which, if they are not desired, disappear in the course of time when stored in room temperature. This can be IR-spectroscopically observed.

The preparation of the fibres of the invention is described more detailed by means of an exemplary embodiment.

Example

The educts TEOS (tetraetoxysilane), EtOH, H₂O ja HNO₃ are mixed in the molar ratio of 1 : 1,26 : x : 0.01 (with x = 1,6, 1,7, 1,8, 1,9 and 2,0) and stirred intensively 5 hours in room temperature. The resulting solvents are placed in open dishes in a water bath warmed up to 70° C, wherein they remain until to a defined weight loss. After that it is cooled and filtered through a refined steel net having a mesh size of 1 mm x 1 mm. The filtrate is subjected to an aging time of from 6 hours to 6 months depending on the weight loss in a closed dish at a temperature of 3°C. The resulting spinning mass is very homogeneous and stable and spinnable for some time.

The preparation of fibres is performed in a dry-spinning device. The spinning mass is filled into a spinning head cooled to -15°C under a pressure of 10 – 15 bar first through a refined steel net having a mesh size of 80 µm 20 x 80 µm and then pressed through the nozzle having a diameter of 100 µm.

The resulting continuous thread is wrapped after a drying path of 1 m on a rotating cylinder.

The resulting fibres show, depending on the initial mixture, i.e. on the amount of water added, round, oval or bone-shaped cross-section forms having diameters between 5 and 30 µm. The cross-section surfaces are between 100 and 400 µm². The fibre surface is flat and has no wave profile in any case. The tensile strength measurements of the fibres gave values of 100 – 800 Mpa.

IR-spectra made of fibre material show a Si – OH -bond at 950 cm⁻¹ and C – H signals at 3000 cm⁻¹. Also a partially hydrolysed and partially condensated etoxy-silanol-fibre is at hand. After circa 2 months storage in room temperature no more C –H-vibration bonds are to be found in the IR-spectrum.

The fibres have changed to partially condensated silanol-fibres, which are stable over a time period of several months.

Claims

1. Biologically degradable and/or biologically resorbable fibres, which are obtainable by drawing fibres from a spinning mass and their eventual drying, whereby the spinning mass contains one or more partially or completely hydrolytically condensed compounds of silica, which derive by hydrolytic condensation from monomers of the general formula I

SiX_4 (I),

in which rests X are the same or different and stand for hydroxy, hydrogen, halogen, amino, alkoxy, acyloxy, alkyl carbonyl or alkoxy carbonyl and derive from alkyl rests, which are eventually substituted straight-chain, branched or cyclic rests having 1 to 20 carbon atoms, preferably having 1 to 10 carbon atoms and can be interrupted through oxygen or sulphur atoms or through amino groups.

2. Method for preparation of biologically degradable and/or biologically resorbable (continuous) fibres having a flat fibre surface according to claim 1, the method comprising the following characteristic features:
 - preparing a spinning mass by hydrolytic (partial) condensation of one or more Si-compounds of the general formula I and/or precondensates derived therefrom defined in claim 1,
 - performing the hydrolytic condensation, eventually in the presence of a catalyst and/or a solvent by adding water by
 - using such a big amount of water, that the molar ratio $\text{SiX}_4 : \text{H}_2\text{O}$ is between 1 : 1 and 1 : 10, preferably between 1 : 1.5 and 1 : 2.5,
 - using a phase-transfer catalysator or such a big amount of water-soluble solvent (S) or mixture of solvent, that the molar ratio is $\text{S} : \text{SiX}_4 \geq 1$, preferably > 1,
 - removing S after the terminated hydrolysis and adjustment of a dynamic balance until the resulting mixture has in room temperature and in shear rate of 20 s^{-1} a viscosity between 0,05 and 50 Pa·s, preferably between 0,5 and 2 Pa·s,
 - exposing the resulting mixture to filtration after removing the solvent,

- allowing the resulting mixture to stand after filtration until it obtains spinnability,
 - drawing threads from the spinning mass and eventual drying thereof.
3. Use of fibres according to claim 1 as biologically degradable and /or biologically resorbable reinforcement fibres.